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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
JUEDES, AMY E	
ART UNIT	**PAPER NUMBER**
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/789,807	TJOA ET AL.	
	Examiner	Art Unit	
	AMY E. JUEDES	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-29* is/are pending in the application.

4a) Of the above claim(s) *4-7,10-12,16 and 24-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 8-9, 13-15, and 17-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and remarks, filed 8/8/08, are acknowledged.

Claim 1 has been amended.
Claims 1 and 3-29 are pending.

2. Claims 4-7, 10-12, 16, and 24-29 stand withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 1, 3, 8-9, 13-15, and 17-23 are being acted upon.

3. The rejection of the claims under 35 U.S.C. 112 first paragraph for lack of enablement is withdrawn in view of Applicant's amendment to the claims to recite that the method employs a "human" precursor cell.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 8-9, 14, 17-19, and 23 stand rejected under 35 U.S.C. 102(b) as being anticipated by Bernard et al., 1998 (of record).

As set forth previously, Bernard et al. teach a method comprising culturing non-activated monocytes (i.e. a monocytic dendritic cell precursor) with GM-CSF alone in a TEFLON^{tm} culture bag (i.e. a bag comprising PFTE, see page 18-19 in particular). Bernard et al. further teach that the culture system is adherent free, and that the resulting cells express CD1a (see Fig. 2, in particular). Bernard et al. also teach that the monocytes are isolated by apheresis (see page 18 in particular). Bernard et al. further teach contacting the CD1a+ cells with tetanus toxoid (i.e. a bacterial antigen, see page 22 in particular). Additionally, the instant claims are drawn to a method of differentiating dendritic cells employing a dendritic cell precursor (i.e. a method of using a product made by a particular process). Thus, the method by which the monocytic precursor is produced does not carry patentable weight in the absence of a structurally difference (see MPEP 2113). The monocytic dendritic cell precursors of Bernard et al. are the same as those produced by tangential flow filtration. Additionally, while Bernard et al. do not characterize the CD1a+ cells as immature dendritic cells, they must inherently be immature dendritic cells, since they are produced by a method identical to that of the instant claims.

Applicant's arguments filed 8/8/08 have been fully considered, but they are not persuasive.

Applicant argues that Bernard et al. do not disclose a method of differentiating dendritic cells by culturing in GM-CSF alone, but rather disclose culturing monocytes in GM-CSF and IL-4. Applicant notes that the method involving culture with GM-CSF alone is a method of differentiating macrophages, and results in the absence of significant neo-expression of CD1a by the macrophages.

Bernard et al. teach the exact method of the instant claims (i.e., culturing non-activated monocytes with GM-CSF alone in a bag comprising PFTE). Furthermore, as shown in Fig. 2, the resulting cells do express CD1a at approximately 1/2 log higher intensity than the starting population of monocytes. Thus, the method of Bernard et al. results in a cell displaying the exact same structural properties as recited in the instant claims (i.e. a cell having CD1a on the cell surface). As noted by Applicant, Bernard characterizes the GM-CSF only cells as macrophages and notes the absence of a significant neo-expression of CD1a by the macrophages. However, the instant claims are not limited to cells expressing CD1a to a "significant" degree. Moreover, since Bernard et al. have performed the exact method of the instant claims, they must have inherently obtained an immature dendritic cell. The fact that Bernard et al fail to recognize the inherent properties of the resulting cells is not relevant. Failure of those skilled in the art to contemporaneously recognize an inherent property, function or ingredient of a prior art reference does not preclude a finding of anticipation. Atlas Powder Co. v. IRECO, Inc., 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999), see MPEP 2131.01. Furthermore, a reference is no less anticipatory if, after disclosing the invention, the reference then disparages it, see MPEP 2131.04. Thus, the fact that Bernard et al. fail to recognize the cells as immature dendritic cells, or characterize the level of CD1a expression in Fig. 2 as "not significant" is not relevant. The reference nevertheless discloses the method resulting in the production of CD1a expressing cells of the instant claims.

Applicant further argues that since no characterization of the precursor cells following elutriation has been performed, there is no basis for an assertion that precursors isolated by tangential flow filtration and the method of Bernard et al. are the same.

It is noted that Applicant's argument is only relevant to claims 17-18, which recite that the precursors are enriched by tangential flow filtration. It is the examiner's position that the method used to purify a monocyte population does not result in a structural difference in the cell population. Applicant has

not provided any evidence that monocytes purified by tangential flow filtration are structurally different than monocytes purified by centrifugation, as taught by Bernard et al.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1, 3, 8-9, 13-14, and 17-18 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Matera et al., 2000, in view of Bernard et al., 1998(of record).

As set forth previously, Matera et al. teach a method of differentiating dendritic cells comprising providing a population of peripheral blood monocytes that have been selected by magnetic sorting (i.e. non-activated), and contacting said monocytes with GM-CSF in the absence of additional cytokines (see page 30 and 31 in particular). Matera et al. also teach culturing in a serum free medium (see page 31 in particular). Matera et al. further teach that the dendritic cells generated by culture with GM-CSF express CD1a (see page 31 in particular). Additionally, the instant claims are drawn to a method of differentiating dendritic cells employing a dendritic cell precursor (i.e. a method of using a product made by a particular process). Thus, the method by which the monocytic precursor is produced does not carry patentable weight in the absence of a structurally difference (see MPEP 2113). The monocytic dendritic cell precursors of Matera et al. are the same as those produced by tangential flow filtration.

Matera et al. do not teach a low avidity culture vessel comprising PFTE.

Bernard et al. teach a method to generate dendritic cells from purified blood monocytes by culturing in a TEFLON^{tm} (i.e. comprising PFTE) bag. Furthermore, Bernard teaches that said method meets good laboratory practice (GLP) procedures necessary for the clinical use of dendritic cells (see pg. 23).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make the dendritic cells taught by Matera et al., using the TEFLON^{tm} culture vessel, as taught by Bernard. The ordinary artisan at the time the invention was made would have been motivated to do so, since Bernard teaches that this method is useful for clinical purposes, since it involves the large scale differentiation of dendritic cells in a culture system that meets GLP procedures (see abstract and pg. 23). Moreover, one of ordinary skill in the art would have a reasonable expectation of success.

Applicant's arguments filed 8/8/08 have been fully considered, but they are not persuasive.

Applicant argues that Matera et al. disclose that the monocytes cultured in GM-CSF alone are macrophages and not dendritic cells.

As noted by Applicant, Matera et al. teach that monocytes cultured in GM-CSF alone are "macrophage-like cells". Thus, one of ordinary skill in the art would not have a reasonable expectation of success in making an immature dendritic cell by culture with GM-CSF alone. However, the instant claims are not limited to culture with GM-CSF alone, but rather recite that monocytes are cultured with GM-CSF in the absence of additional cytokines. Matera et al. teach culturing monocytes with GM-CSF and the hormone prolactin (i.e. GM-CSF in the absence of additional cytokines) to produce immature dendritic cells. Thus, Matera et al. and Bernard et al. make obvious a method of differentiating dendritic cells that falls within the scope of the instant claims, which are drawn to a method comprising culture with GM-CSF in the absence of additional cytokines.

7. Claims 19-23 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Matera et al. and Bernard et al., as applied to claims 1, 3, 8-9, 13-14, and 17-18 above, in further in view of Bosch et al., 2001 (of record).

As set forth previously, The teachings of Matera et al. and Bernard et al. are described above.

They not teach generating maturing the dendritic cells with IFN-γ and BCG.

Bosch teaches that dendritic cells can be matured with a combination of INF-γ and BCG (i.e. a bacterial antigen). Additionally, Bosch teaches that maturation with IFN-γ and BCG results in a dendritic cell population that can induce an immune response against a tumor antigen in cancer patients (i.e. a therapeutically useful dendritic cell population).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make a dendritic cell, as taught by Matera et al. and Bernard et al., followed by maturation with BCG and IFN-γ as taught by Bosch. The ordinary artisan would have been motivated to do so, since Bosch teaches

that IFN-γ and BCG are extremely potent maturation agents that result in a dendritic cell population that can induce an immune response against a tumor antigen in cancer patients (i.e. a therapeutically useful dendritic cell population). Moreover, one of ordinary skill in the art would have a reasonable expectation of success, since Bosch teaches the effectiveness of these techniques in the generation of dendritic cells.

Applicant's arguments filed 8/8/08 have been fully considered, but they are not persuasive.

Applicant argues that Bosch et al. do not remedy the defects of Matera et al. and Bernard et al. noted above.

However, Matera et al. and Bernard et al. do render the instant claims obvious for the reasons set forth above.

8. Claim 15 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Matera et al. and Bernard, as applied to claims 1, 3, 8-9, 13-14, and 17-18 above, and further in view of Lewalle et al., 2000 (of record).

As set forth previously, The teachings of Matera et al. and Bernard et al. are described above.

They do not teach using a cryopreserved cell population to generate dendritic cells.

Lewalle teaches the generation of dendritic cells from frozen peripheral blood mononuclear cells (see pg. 70). Furthermore, Lewalle teaches that many clinical protocols are based on sequential injections of dendritic cells, and therefore it would be of practical importance to have frozen aliquots of the same peripheral blood mononuclear cells for these purposes (see pg. 70).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make the dendritic cell taught by Matera et al. and Bernard et al., using frozen peripheral blood mononuclear cells, as taught by Lewalle. The ordinary artisan at the time the invention was made would have been motivated to do so, since Lewalle teaches that many clinical protocols are based on sequential injections of dendritic cells (see pg. 70), and therefore it would be of practical importance to have frozen aliquots of the same peripheral blood mononuclear cells for these purposes.
Furthermore, the ordinary artisan would have had a reasonable expectation of success, since Lewalle teaches that dendritic cells derived from frozen peripheral blood mononuclear cells retain their functional capacity (see pg. 73).

Applicant's arguments filed 8/8/08 have been fully considered, but they are not persuasive.

Applicant argues that Lewalle et al. do not remedy the defects of Matera et al. and Bernard et al. noted above.

However, Matera et al. and Bernard et al. do render the instant claims obvious for the reasons set forth above.

9. No claim is allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, Ph.D. whose telephone number is 571-272-4471. The examiner can normally be reached on 6am - 2pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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